Letters

**Complex gastrointestinal anomalies associated with esophageal atresia**

Gastrointestinal anomalies are seen in 22% of patients with esophageal atresia (EA).\(^1\) Associated gastrointestinal anomalies such as duodenal atresia (DA) and imperforate anus (IA) need to be managed urgently\(^1\) because neglect can make esophageal repair difficult for surgeons as well as patients.

We retrospectively reviewed the charts of 98 patients (64 boys) of EA with or without distal fistula who underwent surgery between June 2004 and October 2006 at our tertiary center in southern Iran. Eleven of 98 children (11%) had other associated gastrointestinal anomalies. We assessed the effect of surgeon experience (general or pediatric surgeon), and Waterston class of the patient on the outcome of surgery. Waterston classification is based on the birth weight, severity of pneumonia and associated congenital anomaly.\(^2\)

Four patients died. The major causes of mortality were missed diagnosis in 2 patients, intraoperative bleeding in 1 and early postoperative cardiac arrest in 1. All patients (n=4) with Waterston class C who had appropriate multistage operation survived with no complication, but they had prolonged hospitalization because of heart failure and pneumonia. The patients who presented to our center >48 hours after delivery had pneumonia. Two patients with Waterston A grade, who were managed by a general surgeon, died because of delayed repair of EA (missed diagnosis) and severe pneumonia. Five infants had congenital heart disease, 1 had vertebral anomaly, and 1 had unilateral renal agenesis. Complete patient data are given in Table. Four of 11 patients had EA and DA (G-I), 5 (45%) had EA and IA (G-II), and 2 had EA and DA and IA (G-III).

Associated malformations with EA include anorectal, DA or duodenal stenosis, annular pancreas and ectopic pancreatic tissue.\(^1\) Dave et al\(^3\) reported EA with DA in 4.5% of patients and Ein et al\(^4\) reported duodenal stenosis associated with EA in 9 cases.

The causes of mortality in these patients are multifactorial. Delay in diagnosis and inappropriate initial management contribute to increased morbidity and mortality.\(^1\) Sometimes, associated anomalies have a protective effect though usually they exacerbate one another. The surgeon, who deals with these patients, should thus be familiar with the advantages or disadvantages of associated anomalies.\(^1\)–\(^4\)

The primary simultaneous repair of both anomalies without a gastrostomy is justified but the staged repair (ideally within 1 week) is also reported to be a safe and suitable method of management.\(^3\)–\(^6\) We did not see any relation between the type of anomalies and increase in mortality rate in our patients. Moreover, the interval (>48 hours) from the time of delivery and the start of treatment is associated with severe pneumonia. Although Waterston class is a good predictor of general cardiorespiratory reserve and is a very important milestone for deciding about the type of operation, yet the experience of surgeon as the most important predictor of survival cannot be denied because it not only prevents many delayed or missed diagnoses but also introduces the best option for treatment.

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### Table: Esophageal atresia associated with other congenital and gastrointestinal factors

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (days)</th>
<th>Weight (gram)</th>
<th>Gestational age (week)</th>
<th>Associated anomalies</th>
<th>Waterston class</th>
<th>Type of repair</th>
<th>Complication</th>
<th>Hospitalization (days)</th>
<th>Survived</th>
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<tbody>
<tr>
<td>G-I*</td>
<td>F</td>
<td>2</td>
<td>1800</td>
<td>36</td>
<td>DA, vertebral anomaly</td>
<td>A</td>
<td>ER+DR</td>
<td>Bleeding</td>
<td>3</td>
<td>No</td>
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<td>G-I</td>
<td>F</td>
<td>3</td>
<td>1950</td>
<td>38</td>
<td>DA, VSD, PDA</td>
<td>B</td>
<td>ER, DR</td>
<td>HF</td>
<td>21</td>
<td>Yes</td>
</tr>
<tr>
<td>G-I</td>
<td>F</td>
<td>1</td>
<td>2000</td>
<td>38</td>
<td>DA, VSD</td>
<td>B</td>
<td>ER, DR</td>
<td>-</td>
<td>11</td>
<td>Yes</td>
</tr>
<tr>
<td>G-I</td>
<td>M</td>
<td>4</td>
<td>2100</td>
<td>40</td>
<td>DA</td>
<td>C</td>
<td>GT/ER/DR</td>
<td>Severe PN</td>
<td>23</td>
<td>Yes</td>
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<tr>
<td>G-II</td>
<td>M</td>
<td>4</td>
<td>2000</td>
<td>38</td>
<td>IA, VSD</td>
<td>C</td>
<td>GT, CL/ER</td>
<td>PN, HF</td>
<td>17</td>
<td>Yes</td>
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<tr>
<td>G-II</td>
<td>M</td>
<td>5</td>
<td>2250</td>
<td>39</td>
<td>IA, PDA</td>
<td>C</td>
<td>GT, CL/ER</td>
<td>PN, HF</td>
<td>15</td>
<td>Yes</td>
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<tr>
<td>G-II</td>
<td>M</td>
<td>2</td>
<td>2100</td>
<td>38.5</td>
<td>IA</td>
<td>A</td>
<td>CL/ER</td>
<td>MD, PN</td>
<td>5</td>
<td>No</td>
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<tr>
<td>G-II</td>
<td>F</td>
<td>2</td>
<td>2400</td>
<td>40</td>
<td>IA</td>
<td>A</td>
<td>CL/ER</td>
<td>MD, PN</td>
<td>7</td>
<td>No</td>
</tr>
<tr>
<td>G-II</td>
<td>F</td>
<td>2</td>
<td>1900</td>
<td>38</td>
<td>IA, renal agenesis</td>
<td>A</td>
<td>ER, CL</td>
<td>-</td>
<td>9</td>
<td>Yes</td>
</tr>
<tr>
<td>G-III</td>
<td>M</td>
<td>2</td>
<td>1800</td>
<td>36</td>
<td>DA, IA, TOF</td>
<td>C</td>
<td>GT/ER/DR, CL</td>
<td>PN, HF</td>
<td>28</td>
<td>Yes</td>
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<tr>
<td>G-III</td>
<td>M</td>
<td>1</td>
<td>2000</td>
<td>38</td>
<td>DA, IA</td>
<td>B</td>
<td>ER+GT</td>
<td>Cardiac arrest</td>
<td>2</td>
<td>No</td>
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</tbody>
</table>

*Patients were classified as G-I, II or III depending on the type of anomalies. F Female, M male, DA duodenal atresia, IA imperforate anus, EA esophageal atresia, GT gastrostomy, DR duodenal repair, ER esophageal repair, MD Missed diagnosis, CL colostomy, VSD ventricular septal defect, TOF tetralogy of Fallot, PDA patent ductus, PN pneumonia, HF heart failure
References


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H. heilmannii infection and gastric carcinogenesis

We present, for the first time, a case of H. heilmannii infection associated with adenocarcinoma, which showed an increase in the expression of biomarkers of carcinogenesis compared with gastritis and intestinal metaplasia.

A 74-year-old man, who had no contact with pets, presented with abdominal pain, emesis and melena for two weeks. Endoscopy showed a large 1.5 cm x 3 cm deep ulcer, along the angularis. Gastric ulcer and antral biopsies showed chronic active gastritis and marked intestinal metaplasia, and modified Giemsa stain for Helicobacter was positive. Helicobacter organisms were longer than Helicobacter pylori and curvilinear, consistent with H. heilmannii. Biopsies from the ulcer also showed focally invasive adenocarcinoma. The patient refused surgical resection or chemotherapy. He was treated with amoxicillin 1000 mg, clarithromycin 500 mg and omeprazole 40 mg twice daily for 2 weeks. Repeat endoscopic examination performed 3 months later revealed near-complete healing of the ulcer, but biopsies showed invasive adenocarcinoma in the background of marked intestinal metaplasia. Modified Giemsa stain was negative. Immunohistochemical staining was performed on paraffin-embedded, formalin-fixed biopsies to determine the expression of TNF-α, cyclo-oxygenase (COX)-2, epidermal growth factor receptor (EGFR), which are known to play important roles in the development and progression of gastrointestinal cancers. Appropriate polyclonal antibodies were obtained from Santa Cruz Biotechnology Inc., Santa Cruz, CA. The changes in immunohistochemical staining were scored by an independent pathologist, who was unaware of the clinical picture. There was a marked increase in TNF-α, COX-2 and EGFR expression in areas with intestinal metaplasia and cancer compared with gastritis (Figure).

Histologically, adenocarcinoma of the stomach can be of the intestinal or diffuse type. However, there is a sequential progression from gastritis to adenocarcinoma through intestinal metaplasia. It is generally perceived that H. pylori-associated inflammation plays a role in the development of adenocarcinoma.

One case that showed an association of H. heilmannii infection with gastric adenocarcinoma has been reported.1 This case further supports this association. In addition, our data demonstrate, for the first time, that biomarkers of inflammation and carcinogenesis such as TNF-α, COX-2 and EGFR are markedly elevated in adenocarcinoma and intestinal metaplasia compared with gastritis in this pa-

![Figure: Photomicrograph showing changes in expression of TNF-a, COX-2 and EGFR in biopsies from the patient with H. heilmannii infection with gastritis and intestinal metaplasia (H & E)](image)

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tient. This suggests a probable etiologic role for *H. heilmannii* in gastric adenocarcinoma, although further studies are warranted to establish this cause-and-effect relationship.

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References


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Unusual presentation of intraductal papillary mucinous neoplasm of the bile duct

We report a rare case of intraductal papillary mucinous neoplasm of the bile duct (IPMN-B), a tumor almost identical to its pancreatic counterpart, differing only in its site of origin.

A 60-year-old woman presented with abdominal pain and was diagnosed to have acute pancreatitis. She recovered with conservative treatment. Ultrasonography showed a dilated common bile duct (CBD). Magnetic resonance cholangiopancreatography (MRCP) revealed a dilated CBD with a filling defect at the lower end of the bile duct and a prominent pancreatic duct. Endoscopic retrograde cholangiopancreatography (ERCP) showed a large polypoidal lesion in the lower CBD. No stones were seen. Sphincterotomy and stent insertion were performed after brush cytology. At this time, mucus was seen to extrude from the ampulla. Brush cytology showed evidence of moderate cellular atypia. Intermittent sloughing of the tumor into the biliary tree was attributed as the cause of the recurrent pancreatitis. Local excision was not feasible since the tumor was large and was situated beyond the ampulla.

During surgery, the CBD was found to be dilated with the mass felt at its lower end. No adherence to the portal vein, hepatic artery or surrounding structures was seen, nor were there any evidence of peritoneal or falciform ligament seedlings to suggest an adenocarcinoma. The patient underwent a pancreaticoduodenectomy. Recovery was uneventful. The histopathology report was an IPMN-B with reactive hyperplasia of regional lymph nodes.

Intraductal papillary mucinous neoplasm (IPMN) of the pancreas (IPMN-P) is characterized by intraductal proliferation of neoplastic mucin-containing cells, usually from papillae, leading to cystic dilatation of the pancreatic ducts forming clinically and macroscopically detectable masses.1,2

IPMN-B has been extensively described in the Far East, in association with hepatolithiasis. Microscopically, the tumor appears as innumerable frond-like papillary infoldings composed of columnar epithelial cells lining slender fibrovascular stalks.3 Pathologically, IPMN-B is of two types, viz., columnar and cuboidal. These are regarded as analogous to the intestinal and pancreatobiliary IPMN-P. They are classified into four types based on the degree of dysplasia and differentiation of the lining biliary epithelium such that type 1 shows low-grade dysplasia, while type 4 has stromal invasion as in adenocarcinoma.

IPMN-B usually presents in women in the age group of 50–60 years with symptoms of right hypochondrial pain, cholangitis and obstructive jaundice. Pancreatitis, an important presentation of IPMN-P, is not commonly seen with IPMN-B unless the latter is coupled with a tumor in the pancreatic duct.

Mucobilia is the first and most characteristic sign for diagnosis of IPMN-B.4 It helps differentiate IPMN-B from cholangiocarcinoma. Ultrasonography shows the ‘layer sign’ and duodenoscopy reveals a giant or patulous papilla with extrusion of mucin. Cholangiography not only helps in characterizing the type of tumor, which helps in deciding treatment,3 but also demonstrates a communication between the tumor and the bile duct.5

The treatment for IPMN-B is complete resection. The
role of adjuvant treatment for IPMN-B is yet to be established. Early diagnosis and aggressive surgery are important determinants of long-term survival considering that it is a low-grade malignancy.3

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References


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Fibrosing colonopathy in absence of pancreatic enzyme supplementation in one adult patient with cystic fibrosis

Cystic fibrosis is associated with several serious complications in the lower intestinal tract including rectal prolapse, distal intestinal obstruction syndrome (DIOS), intussusception, Crohn disease, carcinoma, volvulus, (silent) appendicitis, and fibrosing colonopathy (FC).

A 43-year-old woman suffering from cystic fibrosis (genotype: compound-heterozygote F508/R347P) presented to us with a 7-month history of cramping abdominal pain and weight loss of 10 kg during this time. There was no history of blood loss in the stool, altered bowel movement or steatorrhea. She denied fever and vomiting. Her past medical history was only significant for airflow limitation which was treated with inhaled budesonide and salmeterol. As she did not have evidence of exocrine deficiency, she was never advised pancreatic enzyme supplementation.1,2 The exact etiopathogenesis still remains unsolved. Other factors that increase the risk of FC are: intake of histamine-2 receptor blockers, corticosteroids, DNase, or mesalazine.2 Newer reports suggest that FC is an endogenous process3 or may be part of the natural course of cystic fibrosis itself.4,5 Our patient had FC, but she had never been exposed to any of these agents.

This case emphasizes that FC also occurs in the absence of pancreatic enzyme substitution, and could therefore be considered a gastrointestinal complication of cystic fibrosis.

Investigations: Her pulmonary function test showed an FEV1 of 72% predicted and FVC of 93% predicted. Laboratory findings were only remarkable for elevated C-reactive protein level (75.0 mg/L) and leukocyte count of 11.5 x 10^9/L. Hemoglobin concentration was 11.5 g/dL. All other laboratory data, particularly liver function tests, amylase and lipase were within normal ranges. CT scan of the abdomen showed an onion-like tumor in the area of the ascending colon. Colonoscopy showed a non-passable circular stenosis of the ascending colon, approximately 25 cm distal from the right flexure of the colon. Histopathologic examination of the endoscopic biopsies was suspicious of low-grade epithelial dysplasia and malignant disease could not be excluded. At laparotomy, a tumor with a diameter of approximately 10 cm x 15 cm was found in the ileocecal region, which was adherent to the abdominal wall. Right-sided hemicolectomy was performed. Histologically, fibrosing colonopathy with ulcerative inflammation and abscess was found (Figure).

Fibrosing colonopathy is a rare complication of cystic fibrosis and typically seen in pediatric patients. It is believed to have a strong association to high-dose pancreatic enzyme supplementation.1,2 The exact etiopathogenesis remains unsolved. Other factors that increase the risk of FC are: intake of histamine-2 receptor blockers, corticosteroids, DNase, or mesalazine.2 Newer reports suggest that FC is an endogenous process3 or may be part of the natural course of cystic fibrosis itself.4,5 Our patient had FC, but she had never been exposed to any of these agents.

This case emphasizes that FC also occurs in the absence of pancreatic enzyme substitution, and could therefore be considered a gastrointestinal complication of cystic fibrosis.

Figure: Chronic inflammation and abscess formation in fibrosing colonopathy. Chronic inflammation leading to fibrosis and abscess formation can be seen. The abscess wall is partially covered with intestinal epithelium, but diverticulosis is not present. Thick mucinous impacts in crypts leading to dilatation (inlet) and eventual rupture may contribute pathogenetically. (CAB/HE (inlet) staining, x 2.5)

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References


Image

Pseudomelanosis duodeni

A 91-year-old man, with history of chronic obstructive airways disease and on long-term therapy with proton pump inhibitor for chronic indigestion, was referred for endoscopy because of increasing dysphagia.

UGI endoscopy revealed hiatus hernia. The duodenal mucosa showed discrete punctate lesions (Figure 1). Duodenal biopsy showed unremarkable duodenal mucosa apart from the presence of hemosiderin within the duodenal villi (Figure 2). The term melanosis, coined by Virchow in 1857 to describe similar appearance in the colon, as the pigment was considered to be melanin or a melanin-like substance.

Pseudomelanosis duodeni refers to the endoscopic appearance of discrete punctuate black pigmentation of duodenal mucosa, which was initially postulated to represent a form of stored iron. The cause and natural history still remains obscured. Electron microscopy reveals accumulation of ferrous sulphide (FeS) in macrophages in lamina propria. The source of the pigment has been attributed to either gastrointestinal bleeding or iron replacement therapy. Melanosisis has been postulated to be associated with age, hypertension and female gender as well as various medications such as sulphur-containing antihypertensive medications and ferrous sulphate.1,2

Our patient was on oral iron replacement therapy and dietary supplements, which contained lutein and zeaxanthine. One of its ingredients is manganese sulphadioxide.

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Figure 1: Endoscopic picture of duodenal mucosa showing discrete punctate lesions

Figure 2: Duodenal biopsy shows the presence of hemosiderin within the duodenal villi (H&E, x40)